***REMARKS***

Upon entry of the above amendment, Claims 6-11, 13-17 and 25-30 will be pending in this application. Claims 6, 8, 11 and 16 have been amended and new claims 25-30 have been added. No new matter has been added. Claims 1-5, 12 and 18-24 have been canceled without prejudice or disclaimer.

Applicants, by canceling any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants have amended claims 6, 8, 11 and 16 solely to advance prosecution. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Presently pending independent claim 6 has been amended to recite "a pharmaceutical composition comprising a fixed combination of active compounds consisting of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination."

Support for claim 6 as amended can be found throughout the specification and the claims as originally filed. In particular, the "combination of active compounds consisting of the active compound ciclesonide...and the active compound R,R-formoterol..." finds basis in the specification at page 5 of the specification in each of the three examples where the only active compounds present are limited to ciclesonide and

R,R-formoterol. No other active compounds are present in the three example formulations. Therefore, there is basis in the specification to limit the active compounds in the presently claimed compositions and methods to only these two active compounds.

Accordingly, the pharmaceutical composition of Claim 6 has been amended to be directed to only these two active compounds. Applicants respectfully point out, however, that the pharmaceutical composition of Claim 6 can contain additional elements such as excipients and/or vehicles in view of the transitional term "comprising" in Claim 6 which modifies the phrase "A pharmaceutical composition...". See also new Claims 25-27 wherein additional excipients and/or vehicles are claimed. However, no additional active ingredients other than "ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof" may be present in the presently claimed subject matter in view of the transitional phrase "consisting of" which modifies the phrase "...a fixed combination of active compounds...". Claims 7-10, 14-17 and 25-27 depend either directly or indirectly from Claim 6.

Similarly, presently pending independent claim 11 has been amended to recite "a method of treating an airway disease in a patient comprising administering to a patient in need thereof a pharmaceutical composition comprising a fixed combination of active compounds consisting of a therapeutically effective amount of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof,

are present ready mixed in a fixed combination." Support for amended claim 11 can be found throughout the specification and the claims as originally filed. In particular, support can be found at page 5 of the present specification in three examples formulations. Claims 13 and 28-30 depend, either directly or indirectly, from claim 11.

The Examiner will recognize that Claim 11 has been amended to be directed to a method of treating airway disorders comprising administering a pharmaceutical composition comprising only these two active compounds. Applicants respectfully point out, however, that the pharmaceutical composition administered in Claim 11 can contain additional elements such as excipients and/or vehicles in view of the transitional term "comprising" in Claim 11 which modifies the phrase "a pharmaceutical composition...". See also new Claims 28-30 wherein additional excipients and/or vehicles are claimed. However, no additional active ingredients other than "ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof" may be present in the presently claimed subject matter in view of the transitional phrase "consisting of" which modifies the phrase "...a fixed combination of active compounds...".

Claims 8 and 16 have been amended to remove language that the Examiner has alleged is non-enabled. These amendments have been made solely to advance prosecution.

Further, Applicants take this opportunity to comment on the Examiner's statements in the "Response to Arguments" outlined on pages 2-5 of the Official Action. First, Applicants take issue with the Examiner's comment at the top of page 3 that "the features upon which applicant relies (i.e. fixed combination or ready mixed in a fixed

combination) are not recited in the rejected claim(s)." Applicants respectfully direct the Examiner's attention to the amendments to claims 6 and 11 submitted February 20, 2009 wherein the limitations that the Examiner alleges are not present in the claims are clearly underlined.

Applicants also take issue with the Examiner's comments on page 3 of the Official Action. On page 3, 8th line from the bottom of the page, the Examiner asserts that "Calatayud, on the other hand, was provided to demonstrate that the R-epimer of formoterol is highly effective in pharmacological activity and possess (sic) minimal systemic effects." This is clearly erroneous since Calatayud et al. do not even teach the formoterol compound. As such, it cannot possibly be used as a reference to substantiate the Examiner's position.

In view of these clear mistakes, Applicants respectfully request that the Examiner carefully consider the amendments that have been submitted herewith, as well as the teachings of the cited art. The amendments and remarks submitted herein clearly obviate the rejections raised by the Examiner.

In view of the remarks set forth below, further and favorable consideration is respectfully requested and an early allowance of this application is earnestly solicited.

## *I. At pages 5-11 of the Official Action, claims 6-11 and 13-17 have been rejected under 35 U.S.C. §112, 1st paragraph for non-enablement.*

The Examiner asserts on page 5 of the Official Action that "the specification ... does not reasonably provide enablement for such pharmaceutical composition and/or method of treating an airway disease comprising the solvate, physiologically functional

derivative, or the solvate of the physiologically functional derivative of ciclesonide along with the solvate, hydrate, solvate of a salt of R,R-formoterol."

Without making any admission as to the validity of this rejection made by the Examiner against the presently pending claims, and solely to advance prosecution of this application, Applicants have removed the language from all claims that the Examiner has alleged is non-enabled.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

***II. At pages 12-15 of the Official Action, claims 6-11 and 13-17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Magee et al. (U.S. Patent Application Publication No. 2002/0111495) in view of Calatayud et al. (U.S. Patent No. 5,482,934).***

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art to incorporate the R-epimer of ciclesonide, as described in Calatayud et al. into the composition comprising compounds of formula I, ciclesonide and formoterol, as described in Magee et al. to arrive at the presently claimed subject matter.

In view of the following, Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court recently held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U. S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the

marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, 550 U.S. at 417). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

It is submitted that a proper case of *prima facie* obviousness has not been established because, whether taken alone or together, none of the cited references teach or suggest all the limitations of the claims as required by *In re Wilson*. Further, a skilled artisan would never be motivated to modify the teachings of the cited references to arrive at the presently pending claims with any reasonable expectation of success as required by *Amgen Inc. v. Chugai Pharm Co.*

Independent claim 6 is directed to a pharmaceutical composition comprising a fixed combination of active compounds consisting of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a

powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination.

Independent claim 11 is directed to a method of treating an airway disease in a patient comprising administering to a patient in need thereof a pharmaceutical composition comprising a fixed combination of active compounds consisting of a therapeutically effective amount of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination.

The Examiner will note that the pharmaceutical composition of Claim 6 and the method of Claim 11 have each been amended so that no additional active ingredients other than "the active ingredient ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof" may be present in the presently claimed subject matter in view of the transitional phrase "consisting of" which modifies the phrase "...a fixed combination of active compounds...". Applicants respectfully point out, however, that the pharmaceutical composition of Claim 6 can contain additional elements such as excipients and/or vehicles in view of the transitional term "comprising" in Claim 6 which modifies the phrase "A pharmaceutical composition...". See also new Claims 25-27 wherein additional excipients and/or vehicles are claimed. Similarly, the method of Claim 11 encompasses a method of

administering a pharmaceutical composition that comprises additional elements such as excipients and/or vehicles in view of the transitional term "comprising" in Claim 11 which modifies the phrase "a pharmaceutical composition...". See also new Claims 28-30 wherein additional excipients and/or vehicles are claimed.

In contrast, Magee et al. describe the use of a compound selected from a general class of PDE4 inhibitors used in combination with other therapeutic agents, including formoterol and ciclesonide. Accordingly, Magee et al. require the combination of a PDE4 inhibitor with an additional active agent such as ciclesonide or formoterol. The presently pending claims specifically exclude any other active ingredients other than those recited in view of the use of the transitional phrase "consisting of" as it relates only to the active ingredients in the fixed combination. Accordingly, Magee et al. does not "teach or suggest all the limitations of the claims" as required by *In re Wilson.*

Further, a skilled artisan would never be motivated to modify the teachings of the Magee et al. reference to arrive at the presently pending claims with any reasonable expectation of success as required by *Amgen Inc. v. Chugai Pharm Co.* Magee et al. require the presence of a PDE4 inhibitor. Ciclesonide and formoterol are only discussed by Magee et al. as two of many alternative "other therapeutic agents" on pages 98-99 that can be combined with the PDE4 inhibitory compounds. Thus, the ordinary skilled artisan would not be motivated by the teachings of the cited references to eliminate the presence of the PDE4 inhibitor and only include the presently claimed ciclesonide and R,R-formoterol compounds. Even further, nowhere does Magee et al. even describe the use of R,R-formoterol. As such, the Magee et al. reference does not render the presently pending claims obvious.

The Calatayud et al. reference does not remedy the deficient teachings of the Magee et al. reference. Calatayud et al. describes the synthesis of a general class of steroids that read on the structure of ciclesonide. Calatayud et al. also describes the purification of the mixture of epimers to obtain either of the epimers in a proportion of at least 99.9%.

Calatayud et al. do not teach the formoterol compound at all, much less R,R-formoterol. In this regard, Applicants respectfully note the Examiner's comments on page 3 of the Official Action. On page 3, 8th line from the bottom of the page, the Examiner asserts that "Calatayud, on the other hand, was provided to demonstrate that the R-epimer of formoterol is highly effective in pharmacological activity and possess (sic) minimal systemic effects." This is clearly erroneous since Calatayud et al. do not even teach the formoterol compound.

Accordingly, Applicants respectfully submit that a proper case of *prima facie* obviousness has not been established because, whether taken alone or together, none of the cited references teach or suggest all the limitations of the claims as required by *In re Wilson*.

As such, the Examiner has failed to demonstrate a *prima facie* case of obviousness against pending claims 6-11 and 13-17. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

***III. At pages 15-18 of the Official Action, claims 6-11 and 13-17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Keller et al. (U.S. Patent No. 6,645,466) in view of Magee et al. and in further view of Calatayud et al.***

The Examiner asserts that Keller et al. describe dry powder formulations for inhalation containing a pharmaceutically effective carrier, pharmaceutically active compounds and magnesium stearate. The Examiner also asserts that it would have been obvious to one of ordinary skill in the art to substitute the R-epimer of ciclesonide as described in Calatayud et al. into the compositions of Keller et al., and to use the resultant compositions for the treatment of airway diseases as described in Magee et al. to arrive at the presently claimed subject matter.

Applicants respectfully traverse this rejection because a *prima facie* case of obviousness has not been established.

A brief outline of relevant authority is set forth above in Section II.

It is submitted that a proper case of *prima facie* obviousness has not been established because, whether taken alone or together, none of the cited references teach or suggest all the limitations of the claims as required by *In re Wilson*. Further, a skilled artisan would never be motivated to modify the teachings of the cited references to arrive at the presently pending claims with any reasonable expectation of success as required by *Amgen Inc. v. Chugai Pharm Co.*

Independent claim 6 is directed to a pharmaceutical composition comprising a fixed combination of active compounds consisting of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a

powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination.

Independent claim 11 is directed to a method of treating an airway disease in a patient comprising administering to a patient in need thereof a pharmaceutical composition comprising a fixed combination of active compounds consisting of a therapeutically effective amount of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination.

As discussed above in Section II, none of Magee et al. and Calatayud et al., whether taken alone or in combination, teach or suggest all the limitations of the claims as required by *In re Wilson*.

Keller et al. do not remedy the deficiencies of Magee et al. and Calatayud et al. Keller et al. is directed to dry powder formulations for inhalation which contain a pharmaceutically ineffective carrier of non-inhalable particle size and a finely divided pharmaceutically active compound of inhalable particle size. *See* Keller et al. at the Abstract. According to Keller et al., magnesium stearate is used in the dry powder formulations. *Id.*

However, like Magee et al. and Calatayud et al., Keller et al. do not teach or suggest a pharmaceutical composition comprising a fixed combination of active

compounds consisting of the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, in an administration form suitable for inhalative administration by means of a powder inhaler, wherein the active compound ciclesonide or an epimer thereof and the active compound R,R-formoterol or a salt, or hydrate of a salt thereof, are present ready mixed in a fixed combination.

Further, nothing in Keller et al., Magee et al. and Calatayud et al. describe the use of R,R-formoterol. As such, none of Keller et al., Magee et al. and Calatayud et al. describe a "pharmaceutical composition comprising a fixed combination of active compounds consisting of the active compound ciclesonide... and R,R-formoterol..." which are present ready mixed in a fixed combination, as presently claimed.

As such, because there is no teaching of the presently claimed very specific R,R-formoterol compound contained in the cited Keller reference, the ordinary skilled artisan would not be motivated to select this specific epimer with any reasonable expectation of success.

Accordingly, Applicants respectfully submit that a proper case of *prima facie* obviousness has not been established because, whether taken alone or together, none of the cited references teach or suggest all the limitations of the claims as required by *In re Wilson*.

As such, the Examiner has failed to demonstrate a *prima facie* case of obviousness against pending claims 6-11 and 13-17. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

***CONCLUSION***

The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

**THE NATH LAW GROUP**

Gary M. Nath
Registration No. 26,965
Joshua B. Goldberg
Registration No. 44,126
Sheldon M. McGee
Registration No. 50,454
Customer No. 34375

Date: October 21, 2009
**THE NATH LAW GROUP**
112 South West Street
Alexandria, VA 22314
Tel: (703) 548-NATH
Fax: (703) 683-8396
JBG/SMM/ROA3.1009.doc